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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,093	12/19/2001	Franz-Josef Mais	Mo6857/Le 33,762	7790

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EXAMINER
MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 03/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,093	MAIS ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10,11 and 13-18* is/are rejected.

7)☒ Claim(s) *12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to an application filed on 12/9/01. There are nine claims pending and nine under consideration. Claims 10-18 are synthesis claims. This is the first action on the merits. The application concerns the synthesis of 4,6-dichloropyrimidine from 4-chloro-6-hydroxypyrimidine. Both the starting material and the product of Applicants' process are old.

Specification

2. The disclosure is objected to because of the following informalities: in Example 8, line 30, page 8, Applicants indicate that 6-hydroxypyrimidine has reacted. Should this not be 6-methoxypyrimidine? Appropriate correction is required.

Priority

3. Applicant cannot rely upon the foreign priority papers to overcome the obviousness rejection made below in points #5 and #6 because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

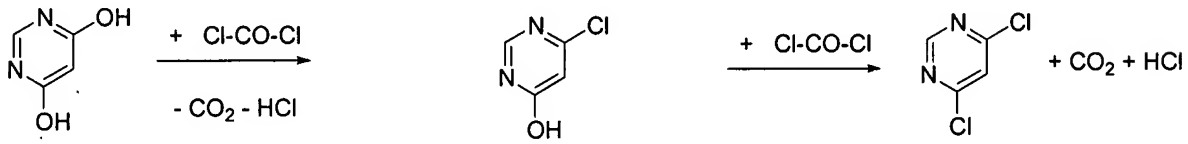
Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 10, 11, and 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Bowen (WO 95/29166 A1). A process is inherently taught if inferences, which one would reasonably make, are taken into account, *In re Napier*, 34 USPQ2d 1782. The reference teaches the reaction of 4,6-dihydroxypyrimidine with phosgene to yield 4,6-dichloropyrimidine. What is inherent in this reference is the use of 4-chloro-6-hydroxypyrimidine as starting material.

The reaction of phosgene or thionyl chloride with a hydroxyl compound requires one molecule of reagent for each hydroxyl group. With phosgene, one molecule of CO_2 and one molecule of HCl must be produced as by-products in the synthesis of a chlorine derivative. Only one hydroxyl group of 4,6-dihydroxypyrimidine may be transformed into a chlorine atom by the phosgene reagent. The reaction taught by Bowen (WO 95/29166 A1), thus may be pictured below. Two molecules of phosgene are required in the process of Bowen (WO 95/29166 A1). Applicants' 4-chloro-6-hydroxypyrimidine starting material is a necessary intermediate in the process taught in the prior art and thus is inherently



4,6-dihydroxypyrimidine 4-chloro-6-hydroxypyrimidine 4,6-dichloropyrimidine

present in the reaction mixture of Bowen (WO 95/29166 A1). Applicants' 4-chloro-6-hydroxypyrimidine starting material is generated *in situ* in the reference. Thus, claim 13, which optionally permits "a reaction mixture containing" the starting material, is inherently anticipated. Since both the starting material and product of Bowen (WO 95/29166 A1) are symmetrical, it is a random choice as to which hydroxyl group first reacts.

The process is found in paragraph 3, page 1, paragraphs 2-8, page 2, and Examples 1-6, pages 2-4 of the reference. Claims 10 and 11 require specific acid chlorides. Phosgene is an acid chloride of formula Cl-CO-Cl. Thus claims 10 and 11 are anticipated. Claims 14 and 15 require use of one equivalent of acid chloride and specific solvents. Line 26 on page 2 of the reference teaches that 2.5 to 3.6 moles of phosgene are required for each mole of starting material. Aromatic, nitrile, ether, and polyether solvents are taught in paragraph 2 on page 2. Thus, claims 14 and 15 are anticipated. Claims 16 and 17 specify temperature and pressure. Reaction temperatures of –10 to 130°C are taught in paragraph 3, page 2 of the reference. The reference is silent as to the pressure used but since the refluxing temperature of methylene chloride is reported as 29°C in Example 2, a pressure of 1 bar may be inferred. Thus, claims 16 and 17 are anticipated.

A process claim is anticipated even if patentee of prior art did not recognize that an "inventive concept" of the new claim was necessarily present, not merely probably or possibly present, in the prior art, *Verdegaal Brothers Inc. v. Union Oil Company of California* 2 USPQ2d 1051. *Mehl/Biophile International Corp. v. Milgraum* 52 USPQ2d 1303, "[i]nherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art."

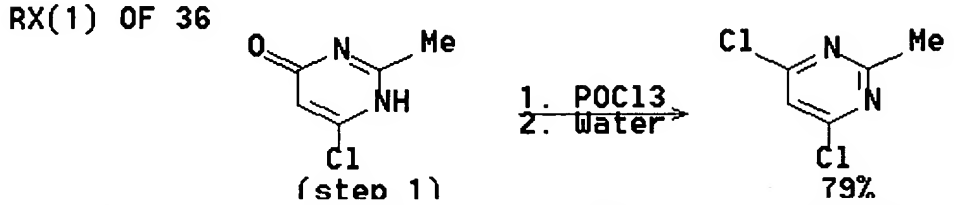
Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 11, 13, 14, and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garner (Heterocyclic Communications) in view of Roberts (Basic Principles of Organic Chemistry). The reference teaches a reaction of 4-chloro-2-methyl-6-hydroxy-pyrimidine with registry number 1780-26-3 with $POCL_3$ shown below. The Applicants claim the reaction of 4-chloro-6-hydroxy-pyrimidine with $POCL_3$. The reference teaches reaction of a compound with methyl group at position 2. The difference between the claimed and taught processes is the extra methyl group on position 2 of the pyrimidine ring. The

process is shown in the reference in Scheme 1, page 504 in the reaction of compound **1** to compound **3**.



The deficiency in the primary reference and the motivation to apply it is provided by Roberts (Basic Principles of Organic Chemistry), "[i]t is well to appreciate, however that a real understanding of organic chemistry involves much *more* than a knowledge of the separate behaviors of classes of compounds with different functional groups. Indeed, it is frequently useful and instructive to consider *types of reactions* rather than *types of compounds"* (paragraph spanning pages 257-258). Roberts (Basic Principles of Organic Chemistry), further says in the final paragraph on page 259, "[s]eparation of functional groups by two or more carbons of a saturated hydrocarbon chain usually serve to insulate them from pronounced interaction, and the properties become more nearly typical of those of the isolated functional groups." The methyl group on the reaction in the prior art is three atoms removed from the site of reaction and does not participate in the chlorination process. While the atoms linking the methyl and oxygen groups are not saturated, methyl is not a functional group, its' steric size is similar to that of

the hydrogen on Applicants' molecule, and a methyl group is not capable of any resonance interaction with the pyrimidine. Thus, it would be obvious to the average synthetic organic chemist to apply the reaction of Garner (Heterocyclic Communications) on a molecule lacking a methyl group to obtain the desired compound as a matter of routine experimentation.

Applicants' process limitations have are characterized above. In lines 7-8, page 504, Garner (Heterocyclic Communications) says, "according to the method of Heinz". Thus, clarification of the conditions employed by Garner (Heterocyclic Communications) is given in Heinz (J. Org. Chem.) in the paragraph spanning pages 1321-1322. Garner (Heterocyclic Communications) employs the acid chloride $POCL_3$. Thus claims 10 and 11 are made obvious. Applicants' claim 13 allows for the starting material to be optionally "used in isolated form". The second sentence of cited paragraph in Heinz (J. Org. Chem.) says "freshly ground". Thus, claim 13 is made obvious. Six equivalents of refluxing phosphorus oxychloride ($POCl_3$), which boils at 106°C, are taught in the same sentence of Heinz (J. Org. Chem.). Thus, claims 14 and 16 are made obvious. Refluxing is an art-recognized term meaning boiling a reaction mixture at atmospheric pressure with return of the condensed material to the reaction vessel. Thus, claim 17 is anticipated. Claim 18 requires addition of starting material to the acid chloride.

The second sentence of cited paragraph in Heinz (J. Org. Chem.) says "was mixed with six equivalents of [$POCl_3$]". Thus, claim 18 is made obvious.

6. In the alternative, Claims 10, 11, 13, 14, and 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Garner (Heterocyclic Communications) alone. The difference between the claim and the prior art process is an extra methyl group on a heteroaryl ring. Two cases have held the obviousness of a methyl-containing ring over a heterocyclic ring lacking a methyl group. In *Ex parte Faugue* 121 USPQ 425, Board of Patent Appeals and Interferences held a methyl furan to be obvious over a furan. The US Court of Custom and Patent Appeals found *In re Miegel* 159 USPQ 716 that a 2,6-dimethylmorpholine was obvious over a morpholine compound. Logically, removal of a methyl group must also be obvious. In the present application, the chemical process claimed is identical to that taught by the reference.

Allowable Subject Matter

7. Objection is made in claim 12 as dependant upon a rejected claim. The following is a statement of reasons for the indication of allowable subject matter: None of the prior art suggests preparing the chlorinating reagent *in situ*. Applicants' claims drawn to the phosphorus containing chlorinating agents are patentable over Jones (GB 2,325,224 A). These phosphorus reagents are capable of delivering two or more chlorine atoms to a target molecule. While it is likely

that Applicants' 4-chloro-6-hydroxypyrimidine starting material is an intermediate in the reaction of 4,6-dihydroxypyrimidine with $POCL_3$ to yield 4,6-dichloropyrimidine as taught by Jones (GB 2,325,224 A), that possibility is not the certainty required by the case law, *In re Rijckaert* 28 USPQ2d 1955, *In re Oelrich* 212 USPQ 323, *In re Robertson*, 49 USPQ2d 1949.

Conclusion

8. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. The FAX number for before final amendments is (703) 872-9306. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, you can reach the Examiner's supervisor, Mukund Shah at (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Thomas McKenzie, Ph.D.
Patent Examiner
Art Unit 1624

TCMcK
February 27, 2003